**REMARKS**

Claims 25-29 are pending in the application. The Examiner has raised the following rejections:

**I.** Claims 25-29 are rejected under 35 U.S.C. §112, first paragraph as as allegedly failing to comply with the written description requirement; and

**II.** Claims 25-29 are rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Cleary, *et al.*, ("Cleary") in view of Levy, *et al.*, ("Levy") and Embleton, *et al.* ("Embleton").

Applicant respectfully requests reconsideration of the application in view comments provided herein. The rejections will be addressed in the order listed above.

**I. THE WRITTEN DESCRIPTION REQUIREMENT IS SATISFIED**

The Examiner has rejected Claims 25-29 under 35 U.S.C. §112, first paragraph as as allegedly failing to comply with the written description requirement (Office Action, page 3). In particular, the Examiner asserts that the claims encompass the administration of entire recombinant cells and further asserts that the specification does not support the administration of entire cells, and that the Applicant was thus not in possession of the invention as claimed (Office Action, page 3).

Applicants respectfully disagree. Analysis of the written description must be applied to the invention as claimed. The claimed invention is to a composition, a cell.

In the instant case, the Applicant was clearly in possession of the claimed cell at the time the application was filed. As the Examiner admits, the specification is directed at "methods for the production of tumor-specific Ig derived from B cell lymphoma." (Office Action page 2, citing page 89, lines 14-15 of the specification). The disclosed methods of producing said tumor-specific Ig derived from B-cell lymphoma involve the creation of a cell expressing a combination of variable regions derived from different

tumor cells (*i.e.*, a multivalent composition). See, *e.g.*, the paragraph starting at page 89, line 19 to page 90, line 2, which outlines the steps of: isolating a mixture of tumor Ig variable regions; cloning them into an expression vector; and co-transforming them into a cell. Experimental details of the construction of the expression and selection/amplification plasmids and cell transformation are provided, *e.g.*, from page 90, line 3 to page 101, line 5. Methods of verifying that the cells express the cloned Ig proteins are described on page 101, lines 7-8. Applicants have thus explicitly demonstrated possession of "A cell expressing a multivalent composition" as is claimed.

Applicant is not required to provide examples of every conceivable method of using the composition in order to demonstrate possession of the claimed composition itself. It is well established that specific examples are not required, and the Federal Circuit has repeatedly confirmed that the absence of examples covering the full scope of the claims does not render the written description inadequate to show possession of the invention. As the court recently affirmed:

> "A claim will not be invalidated on section 112 grounds simply because the embodiments of the specification do not contain examples explicitly covering the full scope of the claim language. That is because the patent specification is written for a person of skill in the art, and such a person comes to the patent with the knowledge of what has come before. Placed in that context, it is unnecessary to spell out every detail of the invention in the specification; only enough must be included to convince a person of skill in the art that the inventor possessed the invention and to enable such a person to make and use the invention without undue experimentation."

*Falkner, Holzer and Dorner v. Inglis, Boursnell, Minson,* 448 F.3d 1357, (Fed. Cir. 2006), citing *LizardTech, Inc. v. Earth Resource Mapping, PTY, Inc.*, 424 F.3d 1336, 1345 (Fed. Cir. 2005).

To the extent that one of skill in the art at the time of filing would interpret the claims to encompass a cell that could be used directly in immunotherapy, as the Examiner has asserted, Applicant submits that the same person of skill in the art would conclude that Applicant's disclosure demonstrates possession by the inventor of a cell

suitable for such use. Nonetheless, this *method* is not the subject matter of the instant claims, and is thus irrelevant to determining possession by the inventor of the claimed *composition*.

For the reasons recited above, Applicant submits the requirements of 35 U.S.C. §112, first paragraph are satisfied with respect to Claims 25-29, and respectfully requests that this rejection be withdrawn.

## II. THE CLAIMS ARE NOT OBVIOUS

The Examiner has rejected Claims 25-29 under 35 U.S.C. §103(a) as allegedly being unpatentable over Cleary in view of Levy and Embleton.

Prima facie obviousness requires: 1) a suggestion or motivation in the references or the knowledge generally available to combine or modify the reference teachings; 2) a reasonable expectation of success should the suggested combination or modification take place; and 3) a teaching or suggestion of all the limitations of the claims. A showing of obviousness will fail if any one of these elements is not met. See, *e.g.*, MPEP § 2143. Applicant submits that the combination of the Cleary, Levy and Embleton references fails to establish obviousness of the claimed invention.

While not acquiescing that the other requirements for a showing of obviousness are met, Applicant submits that the combination of references fails to establish obviousness for the following reasons:

**A.** The combination fails to teach each and every element of the instantly claimed composition.

**B.** The references teach away from making such a combination.

### A. The references fail to teach each and every element of the instant claims.

The cell or clone "expressing a multivalent composition" claimed in each of Claims 25, 28, and 29 is necessarily a T-lyphoid cell that has been transformed to contain at least two different vectors (an expression vector and an amplification vector and/or selection vector) and genes encoding a mixture of Ig variable regions that are derived from at least two different tumor cells. The claimed cell has these properties because it is

produced by a process that requires, among other things, the following:

a. a plurality of $V_L$ regions;

b. a plurality of $V_H$ regions;

c. at least one expression vector into which said pluralities of $V_L$ regions and $V_L$ regions are inserted

d. a T-lymphoid cell, into which the at least one expression vector is transformed, along with an amplification vector having a specific composition;

e. that the transformed cell is exposed to a particular aqueous solution, so as to identify a particular transformed cell;

f. that the particular transformed cell identified in (e) has the features of:

i. being capable of growth in the aqueous liquid of (e);

ii. express a particular mixture of $V_L$ and $V_H$ regions that necessarily are derived from at different tumor cells, as indicated by the recited combinations of different idiotopes.

The references cited by the Examiner, whether taken alone or in any combination, do not teach any of elements (a)-(f), listed above, nor do they teach or suggest a T-lyphoid cell that that has been transformed to contain at least two different vectors, and to express variable regions derived from at least two different tumor cells. It is well established that individual B-cells express only a single $V_H$ allele and a single $V_L$ allele. Thus, co-expression of at least two $V_H$ regions that differ by at least one idiotope necessarily requires co-expression of $V_H$ regions derived from *different* tumor cells. The same applies to co-expression of $V_L$ regions that differ by at least one idiotope.

The Examiner asserts that one of skill in the art would be motivated to use a multitude of different clones processed according to the method of Embleton to provide the diversity of Ig found a patient having a quasi-clonal B-cell lymphoma. Applicants submit that, were one of skill in the art to use such a multitude of clones processed according to the method of Embleton, one would fail to produce the invention as claimed. The claims are directed to an individual cell expressing the recited multivalent composition. The steps of the claims specify that the identified transformed cell must

express the recited combination of Ig variable regions (see, *e.g.*, step (f) of claim 25, step (h) of Claims 28 and 29). The method of Embleton does not produce an individual cell that expresses a multivalent composition. As such, this combination of references fails to teach each every element of the claimed invention.

**B. The References Teach Away From the Combination.**

The present claims are drawn to an individual cell that is recombinantly engineered so as to co-express $V_H$ and $V_L$ regions from a mixture of *different* tumor cells. The Embleton method has precisely the opposite purpose. Embleton teaches methods of preserving the natural pairings of $V_H$ and $V_L$ regions, specifically by amplifying immunoglobulin genes within single cells, so as to avoid mixtures comprising the DNA of mixed populations of cells. See, *e.g.*, Abstract and second column on page 3831. The Examiner notes that one of the benefits of Embleton is that it avoids the problems with screening of artificial combinations of variable regions (Office Action page 5). In view of such teachings, one of skill in the art would hardly be motivated to use the teachings of Embleton for the purpose of creating an individual cell that intentionally contains DNA from a mixed population of cells, and that intentionally co-expresses artificial combinations of variable regions, as is claimed herein.

The compositions of the instant claims, made by methods recited therein, are not directed at preserving natural pairings of $V_H$ and $V_L$ regions. The instantly claimed composition is made using steps directed at making a single cell that expresses multivalent composition by *combining* the nucleic acid isolated from a mixed population of cells. See, *e.g.*, steps (b) of Claims 25, 28, and 29.

Furthermore, the instantly claimed composition is directed at an individual transformed T-lymphoid cell that co-expresses variable regions derived from different cells. Embleton provides no teaching whatsoever that suggests DNA from different tumor cells should be co-expressed within a single transformed cell. In fact, co-expressing the mixture of variable regions recited in the instant claims is directly contrary to the teachings of Embleton.

Given that the entire purpose of the Embleton method is contrary to the objective of the method steps recited to produce the instantly claimed compositions, Applicant submits that Embleton teaches away from the combination with Cleary and Levy.

For the reasons recited above, Applicant submits that the combination of Cleary, Levy, and Embleton does not establish obviousness of the instant claims and respectfully requests that these rejections be removed.

**CONCLUSION**

For the reasons set forth above, it is respectfully submitted that all reasons for rejection should be removed and Applicant's claims should be passed to allowance. Should the Examiner believe that a telephone interview would aid in the prosecution of this application, Applicant encourages the Examiner to call the undersigned collect at (608) 218-6900.

Dated: November 9, 2006

Mary Ann D. Brow
Registration No. 42,363

MEDLEN & CARROLL, LLP
101 Howard Street, Suite 350
San Francisco, California 94105
(608) 218-6900